BLOOD AND BONE MARROW PATTERNS

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GRUNE & STRATTON, New York and London, 1957



Contents

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Preface

In preparing this material for publication, it was the purpose of the authors to present, by means of colored photomicrographs, blood cell patterns as seen by bone marrow aspirations in various abnormal conditions. It was our intent and desire to emphasize blood cell patterns rather than cell morphology, for by virtue of graphically demonstrating these patterns in conjunction with briefly-worded, salient diagnostic points, it was felt that this atlas would fill a need not met by standard texts and atlases. Through recognition of patterns, the diagnostic value of bone marrow aspirations may be realized. As this helpful procedure no longer lies solely in the realm of the specialist, and predicated upon the idea that this atlas would be of particular value to the nonspecialist practitioner, the student, and the technologist, the first portion of the book has been devoted to the identification of the individual cells so that cell patterns may be more readily recognized.

The technic of exemplifying these patterns by colored photomicrographs with a minimum of text has been used throughout, as in the authors' experience this has proved to be the most valuable teaching method. With the thought that this atlas should be convenient for ready reference at the microscope, the legends to each group of color plates were placed on the facing page. These legends also constitute the entire text and outline the important diagnostic points for recognition of the pattern characteristic of a given hematologic disorder It is hoped that this form of presentation will be adaptable to the training program of other hematologists. Finally, emphasis in appropriate cases has been placed upon bone marrow patterns as well as peripheral blood patterns because it has been our experience that marrow examination may prove decisive in the differential diagnosis of many disease entities. It is not our contention that this book presents a complete classification of all the hematologic disorders, but rather that it represents most of the diseases the physician will encounter in his practice.

Like so many efforts, this was an enterprise made possible by the cooperation and consideration of many individuals. When Drs. Talbott and Li discussed the format of this book, they were indebted to Drs. E. H. Falconer, Stacey Mettier, S. P. Lucia and Byron Hall and especially Dr. Allan McGrath, Jr. Later, as Dr. Talbott and Lieutenant Hunsicker produced this book, they were indebted to General Edwin Rawlings, Commanding Officer of the Materiel Command; Colonel Jack Bollerud, Chief, Aeromedical Laboratories; Colonel Edgar Olson, Chief, 2750th U.S.A.F. Hospital; Colonel Robert Gould, Chief, Orientation Group, Wright-Patterson Air Force Base; and especially Mr. Thomas Lowcher and Mr. Fred Holder, as well as Mr. Steve Saliga, of the Orientation Group at Wright-Patterson Air Force Base. Mr. Lou Zarem, Public Information Officer at Wright Air Development Center, was of great help in arranging for the publication of this book. Special mention must be given to Mr. Harold Tomlin and Sergeant John Blotner, the two men responsible for the photographs in this atlas. Without their patience and untiring efforts, this work could not have been accomplished. Throughout this entire project, Mrs. G. Douglas Talbott's editing and technical help has been of invaluable assistance.

Lastly we are deeply indebted to all our kind friends who made available their slides for these photomicrographs.

The Authors

RED BLOOD CELL SERIES

(1) Rubriblast:

a. Round, large nucleus occupies almost entire cell.
b. Fine, compact chromatin network.
c. Nucleus contains blue nucleoli (uneven blue-colored chromatin).
d. Cytoplasm is a dark blue.

(2) Prorubricyte:

a. Coarser structure of chromatin.
b. The nucleoli still may be distinguished.
c. The cell is slightly smaller than the rubriblast.

(3) Rubricyte:

a. Coarse, lumpy radial structures.
b. Nucleoli are no longer visible.
c There is a dark-blue cytoplasm which lacks any red color.

(4) Metarubricyte:

a. The nucleus is smaller.
b. The cytoplasm is violet to reddish hue.
c. The cytoplasm has a wider band than the nucleus.

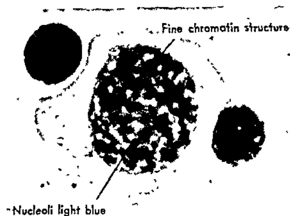
(5) Nucleated red cell:

a A round nucleus coarse and lumpy
b Cytoplasm now red and broad

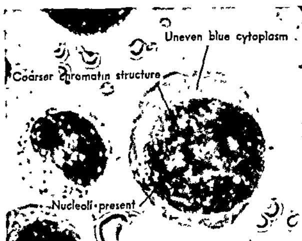
(6) Mature red cell:

a Nucleus no longer visible.
b. Flat, biconcave disc with a reddish hue.

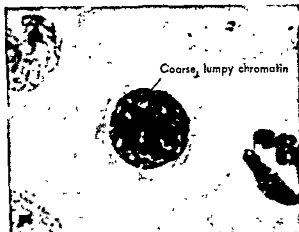
RED BLOOD CELL SERIES



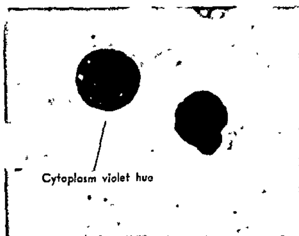
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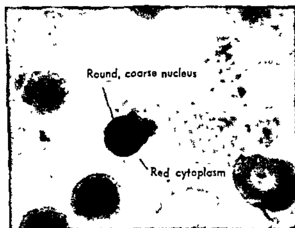
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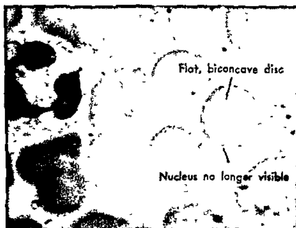
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MYELOCYTES

(1) Myeloblast:

a. Nucleus is round but smaller in relation to the cytoplasm and some of the other cells.

b. Contains moderate amount of chromatin, arranged in clearly defined convoluted network.

c. Nucleus has 2 to 6 nucleoli, surrounded by a border of chromatin.

d. The cytoplasm is broad, light-blue color; no granulation.

(2) Promyelocyte:

a. There are a few azurophilic granules.

b. The nucleoli are clearly visible.

(3) Myelocyte:

a. The size of the nucleus is decreased.

b Nucleoli no longer visible.

c. Cytoplasm pink; no azurophilic granulation

(4) Neutrophilic metamyelocyte:

a. Nucleus slightly indented.

b Chromatin closer but still loose.

c. The cytoplasm is pink.

(5) Stab form:

a The nucleus is indented and slender

b The cytoplasm is pink

c The chromatin network is firmer

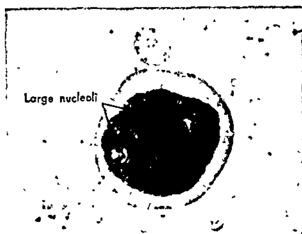
(6) Segmented nucleus:

a. Chromatin compact and lumpy.

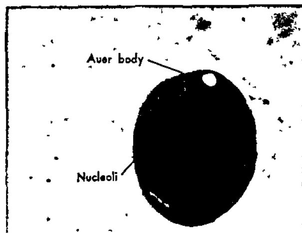
b. Post - nucleolar chromatin masses present.

c. Nucleus elongated, with 2 to 4 segments

MYELOCYTES



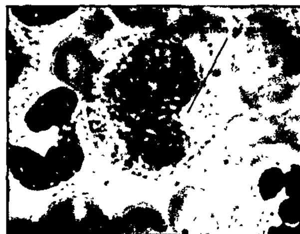
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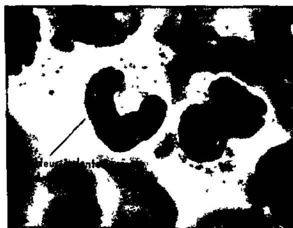
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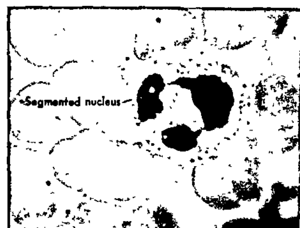
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EOSINOPHILS

(1) Eosinophilic myelocyte:

a. Cytoplasm is pink.
b. Azurophilic or eosinophilic granules present in addition to numerous achromatic dots.
c. Nucleoli are not present.
d. Cytoplasm border small in relation to large nucleus.

(2) Eosinophilic metamyelocyte:

a. The nucleus is slightly indented.
b. The structure is relatively loose.
c. The nucleus is smaller and the cytoplasm larger.
d. Cytoplasm packed with eosinophilic granules.

(3) Mature eosinophil:

a Segmented nucleus connected by several filaments, which usually are short.
b The nucleus has only 2 segments, pouch-shaped — while the neutrophils usually have 3 segments
c There is an abundance of pink cytoplasm with many eosinophilic granules

BASOPHILS

(4) Basophilic myelocyte:

a. The nucleus is round.
b. The cytoplasm is already bluish-pink.
c. There are many granules present.
d. It is of relatively small size, compared with the neutrophils and eosinophils, in this stage of development.
e. The nucleoli are no longer present.

(5) Basophilic metamyelocyte:

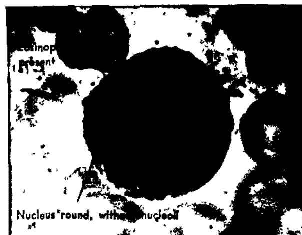
a. The nucleus is indented but segmentation has not yet occurred.
b. Nucleus remains oval in shape.
c. There are specific coarse, metachromatic granules.

(6) Basophils:

a The nucleus has various degrees of segmentation.
b. There is a clover-leaf form—often in a lumpy mass.
c. The cytoplasm is pink.
d. There are large, coarse metachromatic granules present.
e. These granules are larger than in the basophilic metamyelocyte stage.

EOSINOPHILS

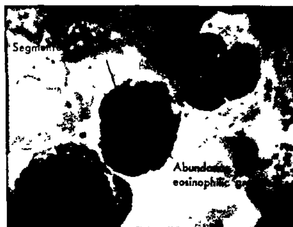
BASOPHILS



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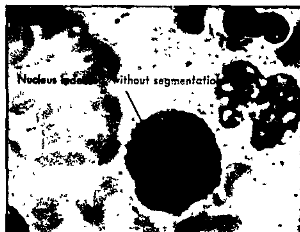
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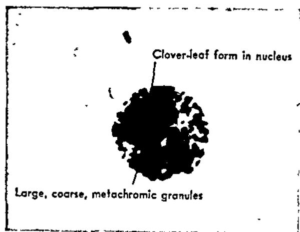
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MONOCYTES

(1) Monoblast:

a The nucleus is round, sometimes indented.
b The chromatin is fine, with a broad and indistinct border.
c The small nucleoli are visible
d The amount of cytoplasm varies and is ungranulated.

(2) Promonocyte:

a. The nucleus is round but may be indented.
b. The nucleoli are no longer visible.
c The cytoplasm is more abundant

(3) Monocyte:

a The nucleus is indented with 2, 3 or more lobes
b The nucleus has little chromatin and loose structure
c There are no nucleoli present
d The cytoplasm is dull, pigeon-blue in color, with dense clouds of fine azurophilic granules

MEGAKARYOCYTES

(4) Megakaryoblast:

a. The nucleus is round — chromatin scanty without characteristic particles
b. The nucleoli are small and indistinct.
c. The cytoplasm is moderately basophilic.
d. May have diploid, tetraploid or octoploid nuclear structures

(5) Promegakaryocyte:

a. There is characteristic polychromic or oxyphilic material.
b. There is one nucleus.
c. The nucleus is indented.

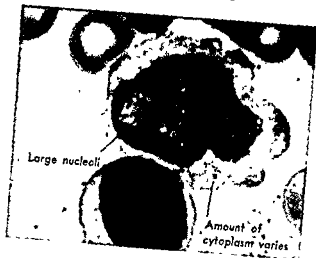
Megakaryocyte:

a. Last stage that is complete cell.
b. Nucleus, numerous indentations — not segmented.
c. Several nucleoli may be present.
d. Cytoplasm has pink, fine, azurophilic granules.
e The granules are throughout the entire cytoplasm.

(6) Blood platelet:

a There are fragments of cytoplasm.
b Azurophilic granules surrounded by a narrow border of ungranulated cytoplasm.

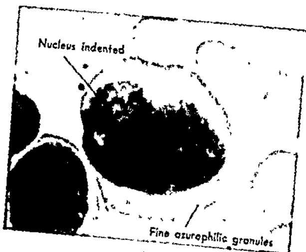
MONOCYTES



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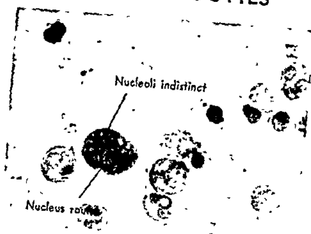


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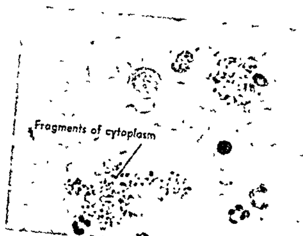
MEGAKARYOCYTES



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PLASMA CELLS

(1) Plasmablast:

a. Round nucleus with dense, concentric chromatin.
b. The nucleoli are difficult to distinguish.
c. The cytoplasm has a narrow border with the nucleus in the center, and is often foamy in appearance.
d. There is no granulation present.

(2) Proplasmacyte:

a. Smaller than the plasmablast.
b. The nucleus is centrally placed, slightly eccentric and several nucleoli are present.
c. There is indistinct chromatin.
d. The cytoplasm has a deep blue color.
e. A pale halo may be present around the nucleus.

(3) Plasmacyte:

a. The cell is elongated.
b. The nucleus is eccentrically located and relatively small.
c. The chromatin may be dark, coarse and cartwheeled in appearance.
d. Pseudopod formation may be present.
e. Chromatin may have the appearance of having vacuolation in it.
f. There are no nucleoli and there is a wide halo about the nucleus.

LYMPHOCYTES

(4) Lymphoblast:

a. Nucleus round—contrasts to other blast cells of the granulocytic series.
b. The structure of the chromatin is faintly visible and lumpy.
c. The nucleus has only one nucleolus, which is characteristically blue and cloudy.
d. The cytoplasm is dark, uneven, with a blue color.
e. There is no granulation.

(5) Prolymphocyte:

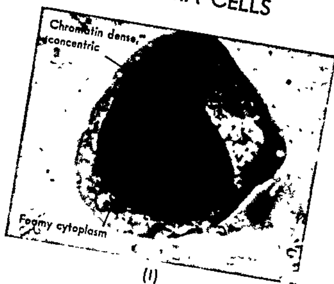
a. Larger cell than lymphoblast.
b. The nucleolus is indistinct.
c The band of cytoplasm surrounding the nucleus is broad.

(6) Mature lymphocyte:

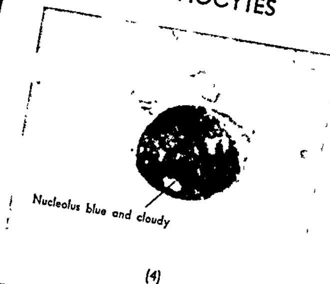
a. The nucleus is round—may sometimes be indented.
b. The chromatin is more or less a dense, lumpy mass.
c The cytoplasm is light blue in color, con[illegible] azurophilic granules surroun[illegible]y halo

PLASMA CELLS

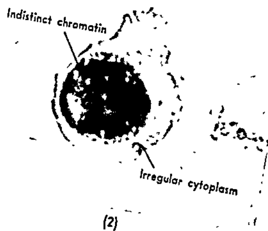
LYMPHOCYTES



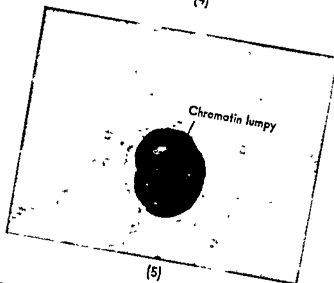
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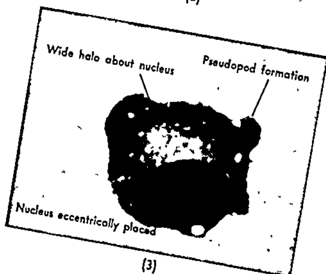
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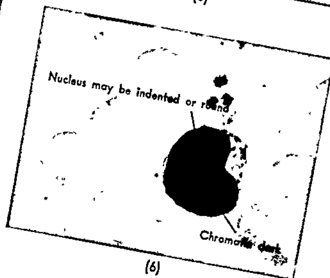
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PERNICIOUS ANEMIA

(1) **Rubricytic hyperplasia of the megaloblastic type:**

a. Marked shift to the left of the red blood series.

b. Prorubricytes predominate.

(2) **Maturation arrest at rubyricytic stage:**

a. Dependent upon stage of anemia.

b. Metarubricytes absent (their presence means recently or inadequately treated pernicious anemia or nutritional macrocytic anemia).

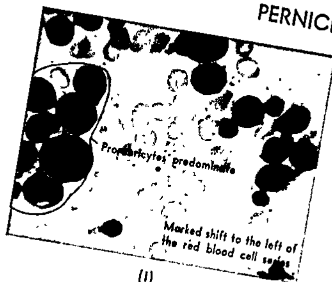
(3) **Giant pernicious anemia type, with band cells present along with hypersegmentation of metamyelocytes.**

(4) **Characteristic open-faced nucleus present in the megaloblastic series. Pseudopods frequently present in blast forms —megaloblastic series.**

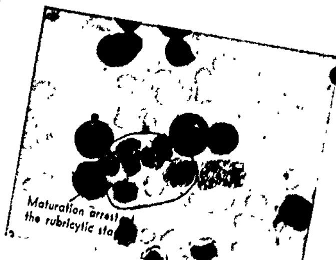
(5) **Variation in size and shape of mature red cells in peripheral blood:**

Difficult to distinguish from other types of megaloblastic anemias, such as nutritional liver disease, sprue, anemia of pregnancy, of infancy, etc

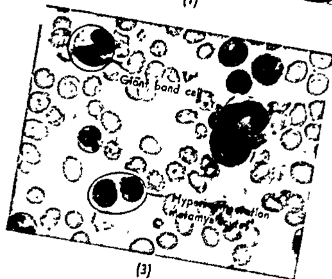
PERNICIOUS ANEMIA



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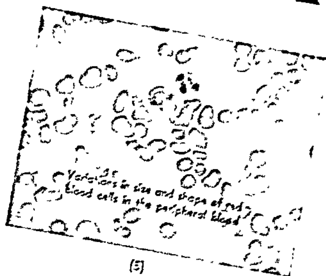
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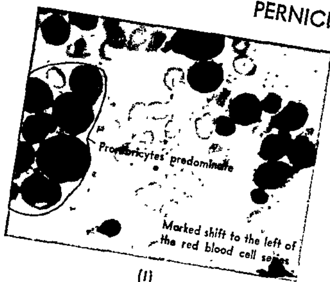
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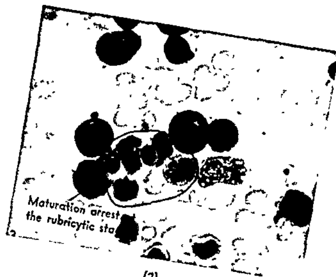
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PERNICIOUS ANEMIA



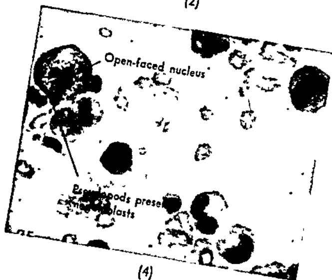
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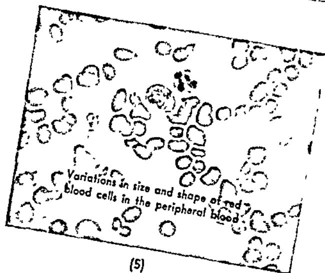
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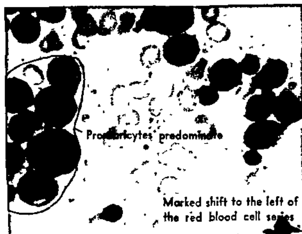
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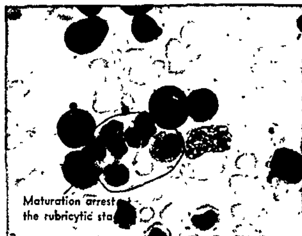
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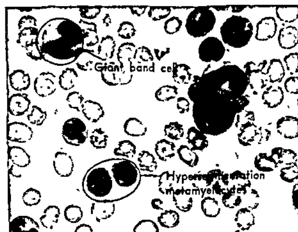
PERNICIOUS ANEMIA



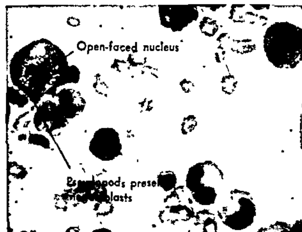
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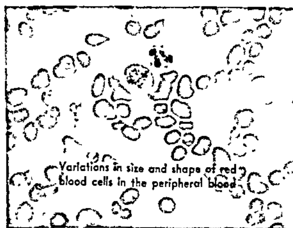
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IRON-DEFICIENCY ANEMIA

(1) Marked shift to the left of the rubricytic series.

(2) Normal maturation of the rubricytic series.

(3) Normal myelocytic series.

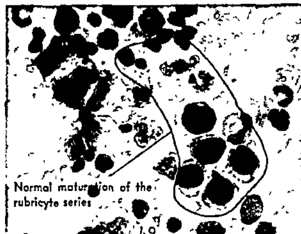
(4) Rubricytic hyperplasia with metarubricytes predominating.

(5) Hypochromia present in the mature red blood cells.

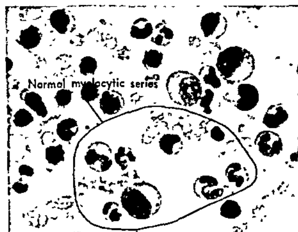
IRON-DEFICIENCY ANEMIA



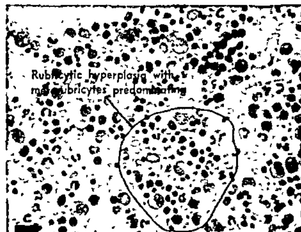
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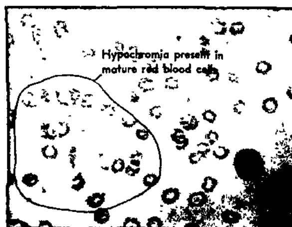
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HEMOLYTIC ANEMIA

(1) Rubricytic hyperplasia—marked shift to the left of the red blood cell series.

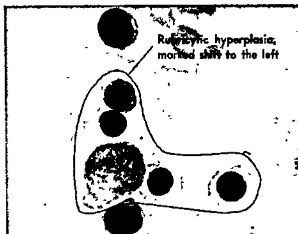
(2) Predominance of rubricytes.

(3) Granulocytic hyperplasia with normal maturation usually accompanies hemolytic anemia.

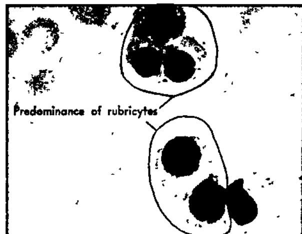
(4) Histiocytes containing ingested red blood cells or hemosiderin are present.

(5) Reticulocytes usually increased.

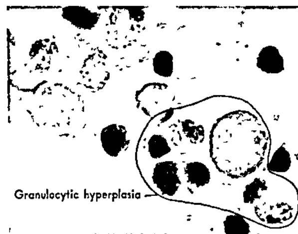
HEMOLYTIC ANEMIA



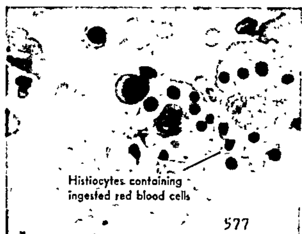
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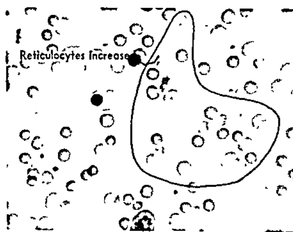
(2)



(3)



(4)



(5)

ERYTHROPHTHISIC ANEMIA

(1) Hypoplastic rubricytic series.

(2) Normal myelocytic elements.

(3) Normal megakaryocytic series.

(4) Anemia usually normochromic, normocytic in type.

(5) Erythrophthisic anemia secondary to:

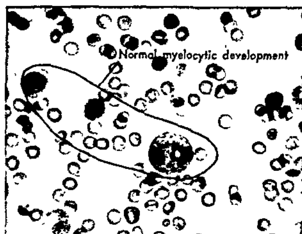
a Congenital defect — born without precursors of the red blood cell series.

b. Hyploplastic marrow from toxic agents — where myelocytic and megakaryocytic elements have recovered.

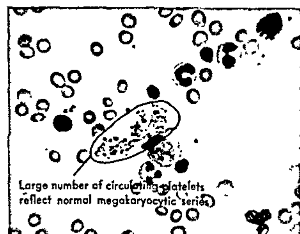
ERYTHROPHTHISIC ANEMIA



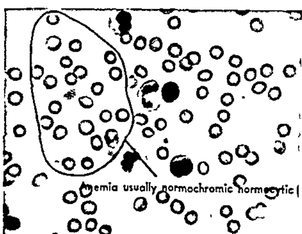
(1)



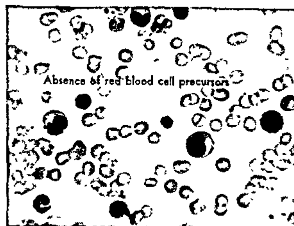
(2)



(3)



(4)



(5)

APLASTIC ANEMIA

(1) Shift to the left of the plasma cell series.

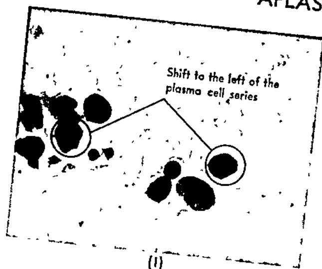
(2) Many young cells of all series are present.

(3) Relative increase of the plasma cell series.

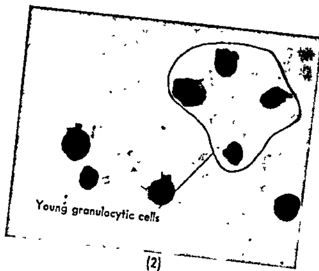
(4) Surgical biopsy of the marrow needed to prove the diagnosis and to rule out aleukemic leukemia and myelofibrosis.

(5) Hypoplasia of all elements:
   a. Rubricytic series.
   b. Myelocytic series
   c. Megakaryocytic series.

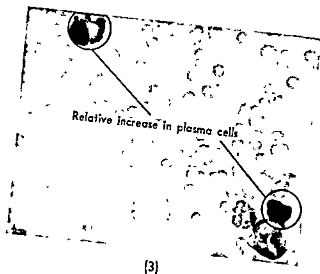
APLASTIC ANEMIA



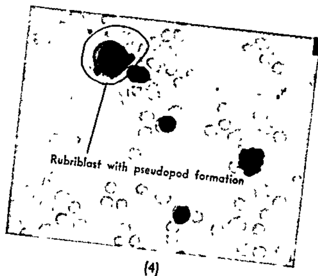
(1)



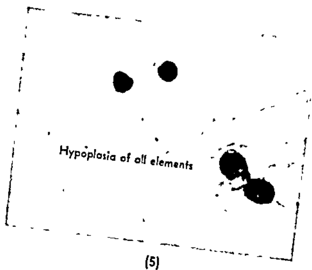
(2)



(3)



(4)



(5)

BLAST CELL LEUKEMIA

(1) Hyperplasia of the diseased cells series:
   a. Blast cells and "pro" cells predominate.
   b. Large nucleoli present.

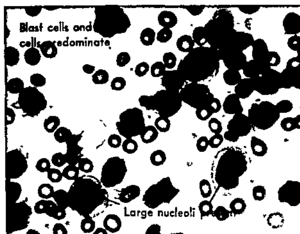
(2) Depression of the megakaryocytic series.

(3) Often difficult to classify the exact type of leukemia, as no mature cells are present except in acute lymphatic leukemia.

(4) Progressive depression of rubricytic series, although early in the disease the red cell elements may be hyperactive.

(5) Undifferentiated early cell forms in the peripheral blood.

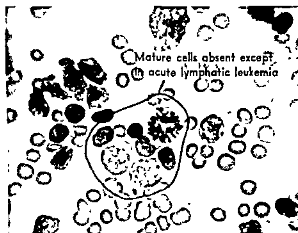
BLAST CELL LEUKEMIA



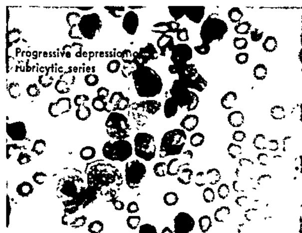
(1)



(2)



(3)



(4)



(5)

ACUTE MYELOGENOUS LEUKEMIA

✓

(1) Marked shift to the left of the myelocytic series.

(2) Young forms of the myelocytic series are present with large *nucleoli. Auer* bodies may or may not be present.

✓

(3) Predominance of promyelocytes and myelocytes.

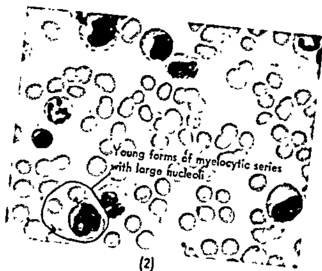
(4) Associated depression of rubricytic elements may be present.

(5) Hiatus leukemicus present in the peripheral blood.

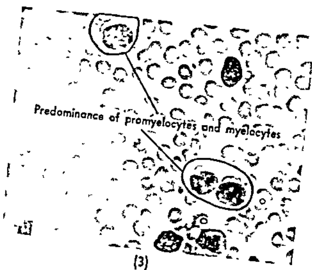
ACUTE MYELOGENOUS LEUKEMIA



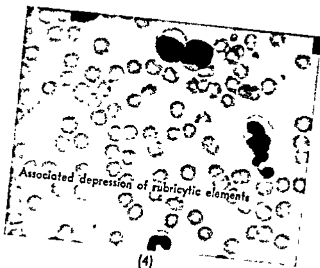
(1)



(2)



(3)



(4)



(5)

CHRONIC MYELOGENOUS LEUKEMIA

(1) Rubricytic series usually depressed. However, early in the disease a polycythemia picture may be seen.

(2) Eosinophils and basophils are increased.

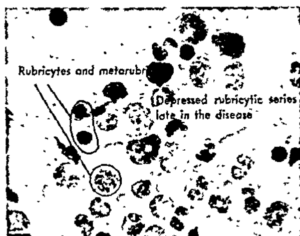
(3) Myelocytic hyperplasia:

a. Moderate shift to the left of the myelocytic series.
b. Myelocytes and metamyelocytes predominate.

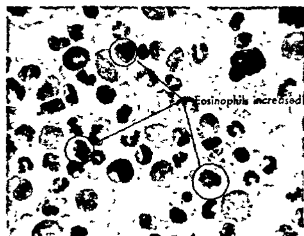
(4) Megakaryocytes and platelets are increased.

(5) Large nucleoli in the myelocytic series may be present even in the late stages.

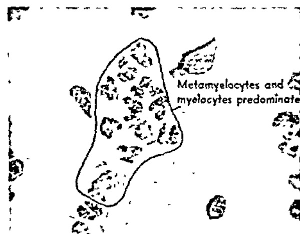
CHRONIC MYELOGENOUS LEUKEMIA



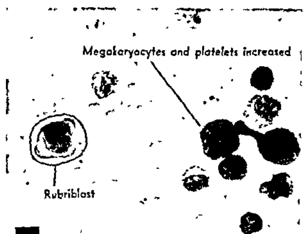
(1)



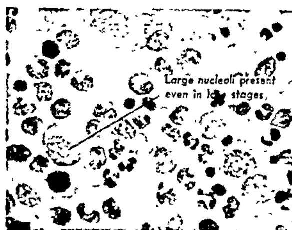
(2)



(3)



(4)



(5)

MONOCYTIC LEUKEMIA (SCHILLING TYPE)

(1) Pseudopod formation and Auer bodies may be present in the early forms.

(2) Histiocytes or reticulum cells frequently present.

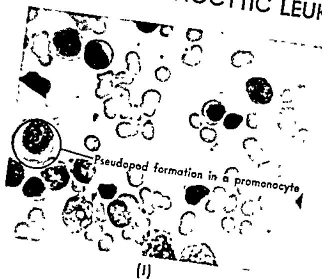
(3) Hypoplasia of the rubricytic and the megakaryocytic series.

(4) Hyperplasia of the monocytic series (with a marked shift to the left.)

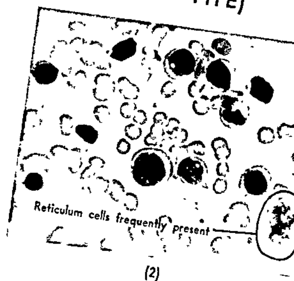
Large nucleoli present in the monoblasts and the promonocytes.

(5) Abnormal young monocytic forms found in the peripheral blood.

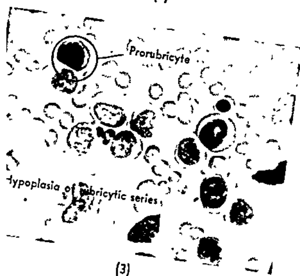
MONOCYTIC LEUKEMIA (SCHILLING TYPE)



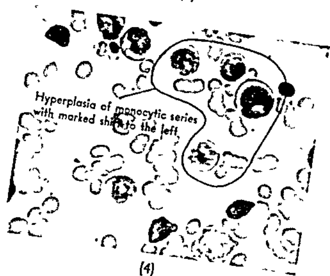
(1)



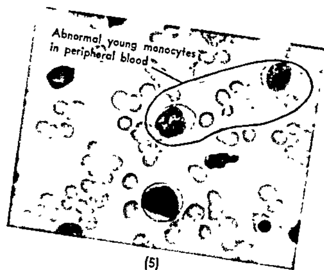
(2)



(3)



(4)



(5)

MONOCYTIC LEUKEMIA (NAEGELI TYPE)

(1) Hyperplasia of the myelocytic and the monocytic séries.

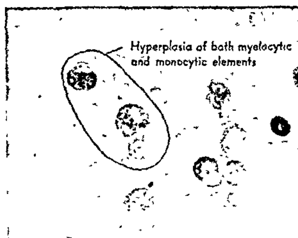
(2) Myelocytic series has normal maturation.

(3) Hypoplasia of the rubricytic and megakaryocytic series.

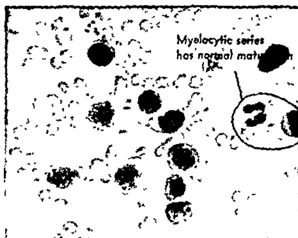
(4) Large nucleoli and pseudopod formation found in the early forms.

(5) Monocytic series demonstrates a shift to the left.

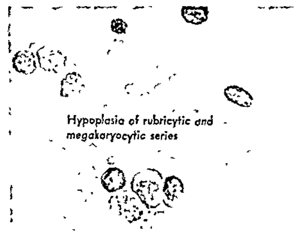
MONOCYTIC LEUKEMIA (NAEGELI TYPE)



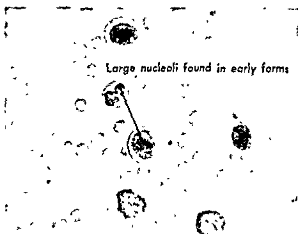
(1)



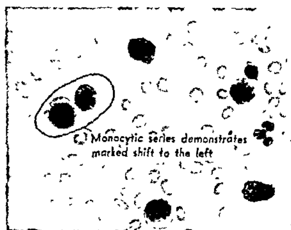
(2)



(3)



(4)



(5)

ACUTE LYMPHATIC LEUKEMIA

(1) Early lymphocytic cells predominate:
a. Large nucleoli in early cell forms.
b. Auer bodies absent in cells.
c. Peroxidase-negative stain demonstrates the prolymphocytes.

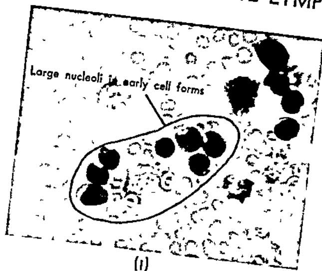
(2) Mature lymphocytes always found in the marrow.

(3) Basket cells present in large numbers.

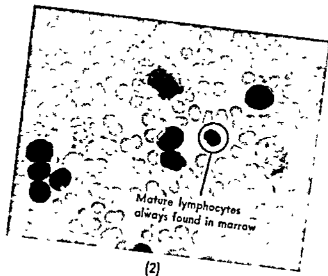
(4) Associated depression of the rubricytic and megakaryocytic series may be present.

(5) Differentiation from other acute leukemias often verified by presence of abnormal lymphocytes in the peripheral blood.

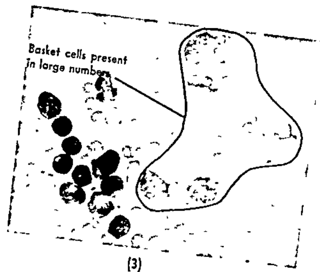
ACUTE LYMPHATIC LEUKEMIA



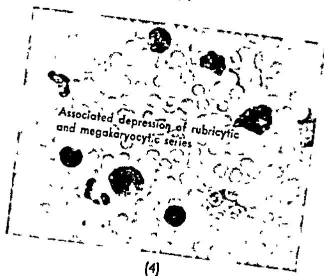
(1)



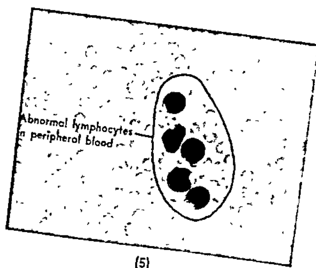
(2)



(3)



(4)



(5)

CHRONIC LYMPHATIC LEUKEMIA

V

(1) Lymphocytic hyperplasia.

Mature lymphocytes predominate; lymphoblasts and prolymphoblasts are present.

(2) Nucleoli found in young lymphocytic cells.

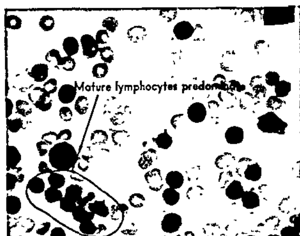
(3) Rubricytic and megakaryocytic series usually depressed.

(4) Basket cells seen in large numbers.

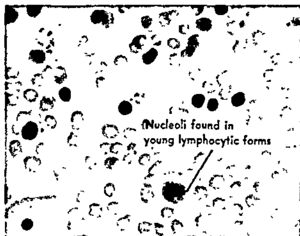
V

(5) Peripheral circulation usually flooded with mature lymphocytes and an occasional immature lymphocytic cell.

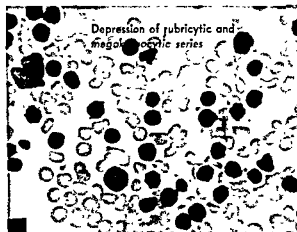
CHRONIC LYMPHATIC LEUKEMIA



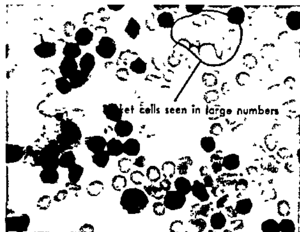
(1)



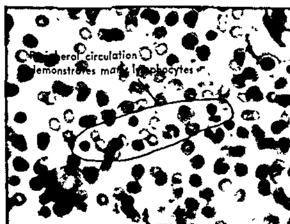
(2)



(3)



(4)



(5)

LYMPHATIC LEUKEMIA (LYMPHOSARCOMA TYPE)

(1) Lymphoblasts and prolymphocytes are present:

a. Large nucleoli.
b. Ragged-edged cytoplasm.

(2) Myelocytic hyperplasia:

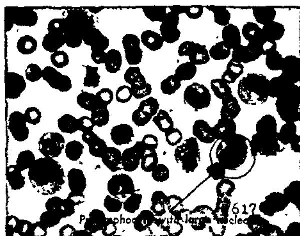
a. No shift to the left.
b. No maturation arrest.

(3) Mature lymphocytes are scarce.

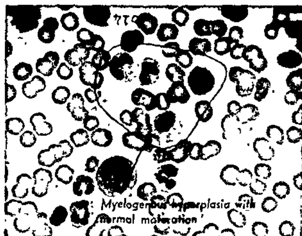
(4) Red cell agglutination.

(5) No peripheral manifestations.

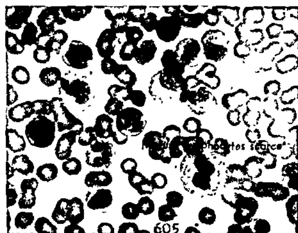
LYMPHATIC LEUKEMIA (LYMPHOSARCOMA TYPE)



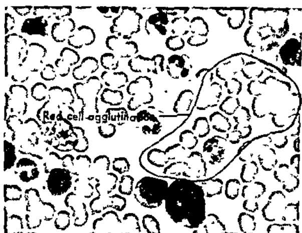
(1)



(2)



(3)



(4)



(5)

GIANT FOLLICULAR LYMPHOMA

(1) Abnormal lymphocytes with pyknotic nuclei are present.

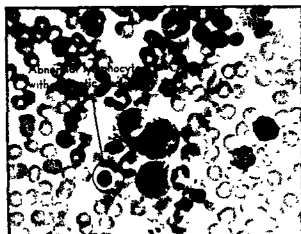
(2) Narrow rim of cytoplasm present in abnormal lymphocytes.

(3) Normal megakaryocytic series.

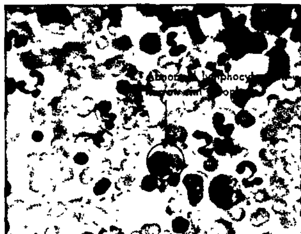
(5) Normal myelocytic series, with peripheral manifestations usually absent.

(4) Rubricytic series may or may not be hyperplastic.

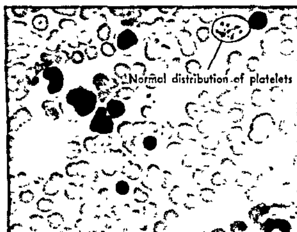
GIANT FOLLICULAR LYMPHOMA



(1)



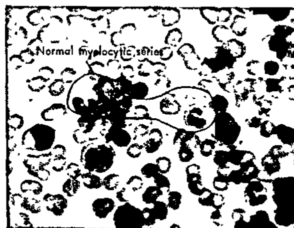
(2)



(3)



(4)



(5)

GIANT FOLLICULAR LYMPHOMA

(1) Abnormal lymphocytes with pyknotic nuclei are present.

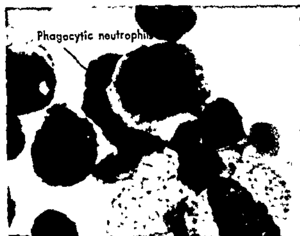
(2) Narrow rim of cytoplasm present in abnormal lymphocytes.

(3) Normal megakaryocytic series.

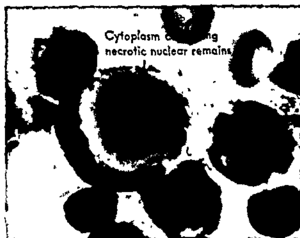
(5) Normal myelocytic series, with peripheral manifestations usually absent.

(4) Rubricytic series may or may not be hyperplastic.

LUPUS CELLS

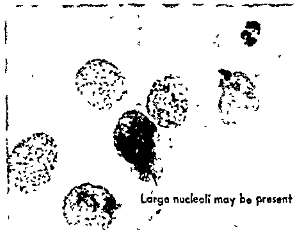


(1)

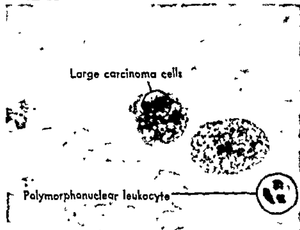


(2)

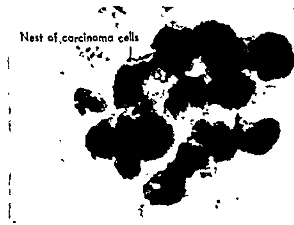
TUMOR CELLS



(3)



(4)



(5)

INFECTIOUS MONONUCLEOSIS

(1) Several types of atypical lymphocytes seen in the peripheral blood.

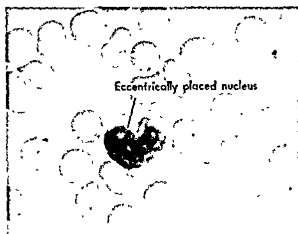
(2) Atypical lymphocytes may have eccentrically-shaped nuclei.

(3) Atypical lymphocytes may have vacuolated, foamy cytoplasm.

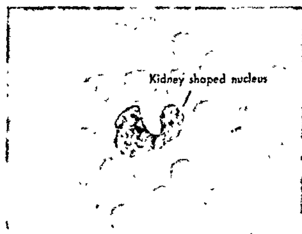
(4) Normal rubricytic and megakaryocytic series.

(5) Myelocytic hyperplasia:
- a. Shift to the left of the myelocytic series.
- b. Promyelocytes increased.
- c. Large nucleoli absent.
- d Abnormal lymphocytes absent in the bone marrow.

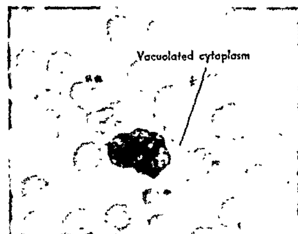
INFECTIOUS MONONUCLEOSIS



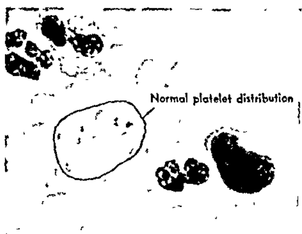
(1)



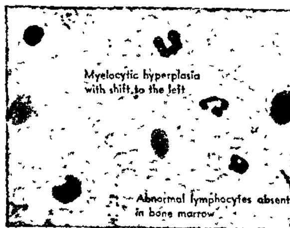
(2)



(3)



(4)



(5)

MULTIPLE MYELOMA

(1) Plasmacytic hyperplasia — double- and triple-nucleated cells.

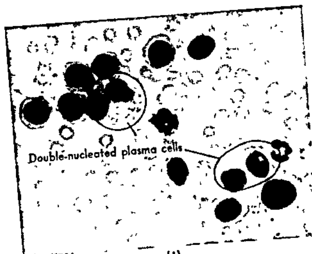
(2) Shift to the left in the plasmacytic series.

(3) Megakaryocytes and rubricytes usually depressed, but occasionally megakaryocytosis may be present.

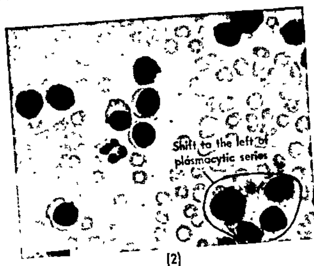
(4) Large nucleoli in the proplasmacytes and the plasmablasts.

(5) Rouleaux formation of the erythrocytes.

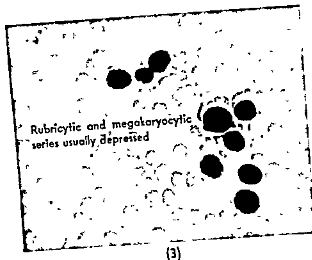
MULTIPLE MYELOMA



(1)



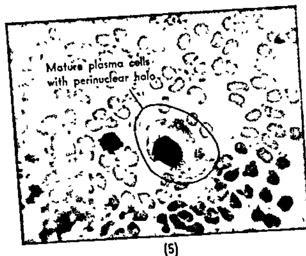
(2)



(3)



(4)



(5)

GAUCHER'S DISEASE

(1) Typical Gaucher cells present in the bone marrow; may be single or grouped in nests.

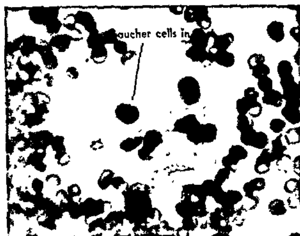
(2) Fibrils in cytoplasm assume circular, concentric or spider-web patterns which distinguish cells from megakaryocytes.

(3) Gaucher cells may be round, oval or spindle-shaped with small, eccentrically placed nucleus.

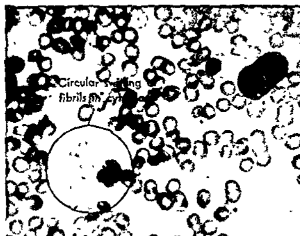
(4) Rubricytic hyperplasia may be secondary to an associated anemia.

(5) Hyperplasia of the megakaryocytic series may be present.

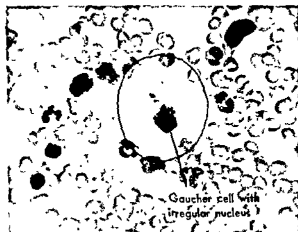
GAUCHER'S DISEASE



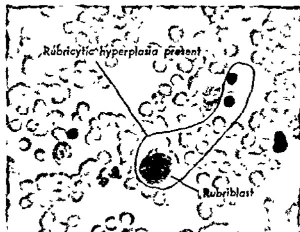
(1)



(2)



(3)



(4)



(5)

POLYCYTHEMIA VERA

(1) No pathognomonic bone marrow pattern.

(2) Early in the disease the patient may have a normal bone marrow pattern.

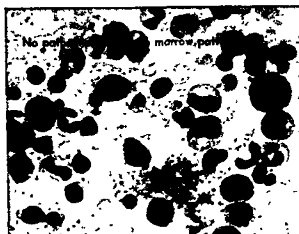
(3) Late sequelae may be chronic myelogenous leukemia, differentiated by the lack of large nucleoli in myeloblasts and promyelocytes.

(4) Later in the disease, the patient may have hyperplasia of all elements:

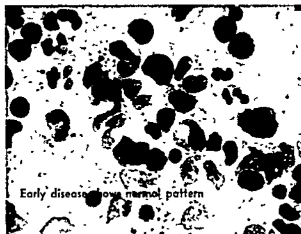
a. Megakaryocytosis.
b. Eosinophilia.
c. Hyperplasia of the myelocytic and rubricytic series.

(5) Late in the disease, the marrow may be hypoplastic.

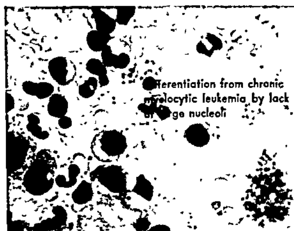
POLYCYTHEMIA VERA



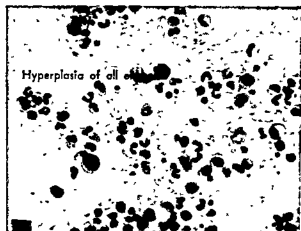
(1)



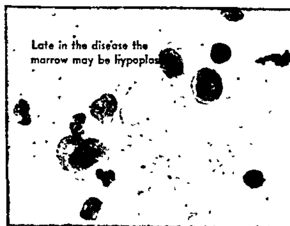
(2)



(3)



(4)



(5)

IRRITATION PHENOMENON

(1) Myelocytic hyperplasia:
  a. Shift to the left of the myelocytic series.
  b Normal maturation.

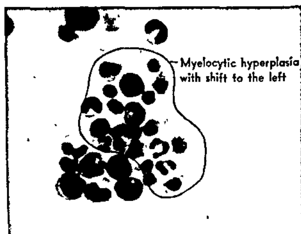
(2) Rubricytic hyperplasia.

(3) Eosinophilia without increase of the basophils.

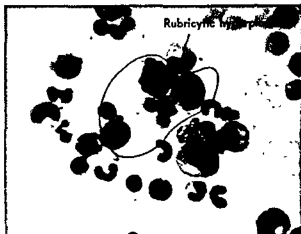
(4) Plasmacytosis and megakaryocytosis.

(5) Irritation phenomenon secondary to:
  a. Metastatic tumor.
  b Septicemia.
  c Rebound phenomenon from depression of marrow, secondary to drug toxicity or x-radiation.

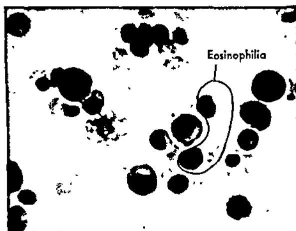
IRRITATION PHENOMENON



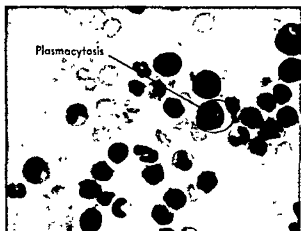
(1)



(2)



(3)



(4)



(5)

IDIOPATHIC THROMBOCYTOPENIC PURPURA

(1) Depressed platelet formation; cytoplasm of megakaryocytes demonstrates few platelets.

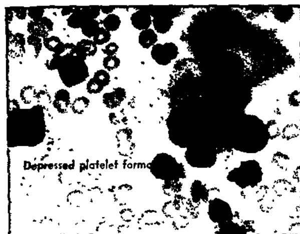
(2) Megakaryocytic hyperplasia.

(3) Maturation arrest of the myelocytic series at the late metamyelocyte or band cell stage.

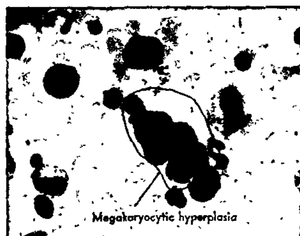
(4) Hyperplasia of rubricytic series secondary to hemorrhage may be present.

(5) Rubricytic series may show a shift to the left, with the presence of many immature forms.

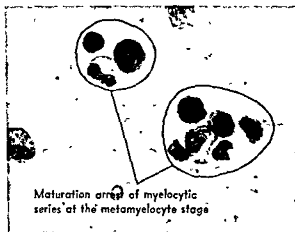
IDIOPATHIC THROMBOCYTOPENIC PURPURA



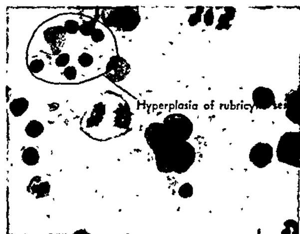
(1)



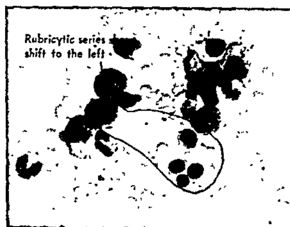
(2)



(3)



(4)



(5)

SPLENIC NEUTROPENIA

(1) Myelocytic hyperplasia.

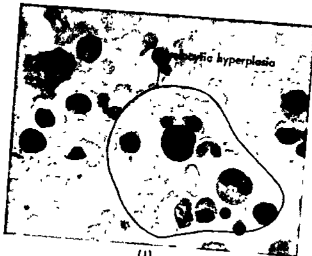
(2) Maturation arrest at the metamyelocytic stage.

(3) Normal rubricytic series.

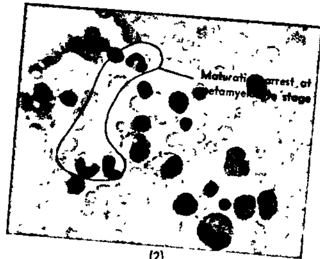
(4) Normal megakaryocytic series.

(5) Normal platelet formation.

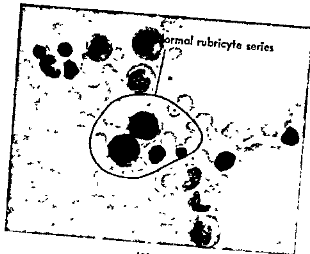
SPLENIC NEUTROPENIA



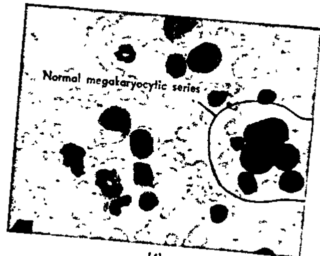
(1)



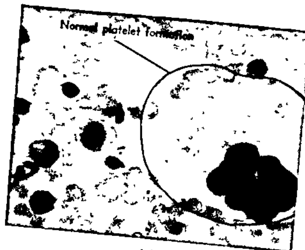
(2)



(3)



(4)



(5)

EXTRAMEDULLARY HEMATOPOIESIS

(1) Shift to the left of the myelocytic series, with immature cells present in the peripheral blood.

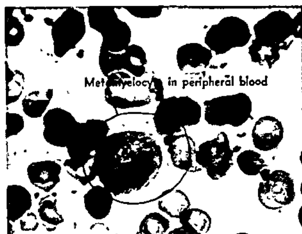
(2) Nucleated red blood cells in the peripheral blood when hemoglobin is 9 grams or less.

(3) Giant platelets and fragments of megakaryocytes in the peripheral blood.

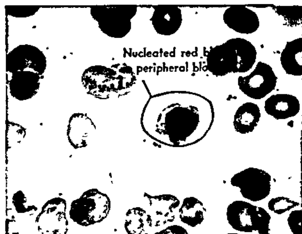
(4) Bone marrow tap will be dry. Condition is present if the marrow is subjected to stress for long period of time.

(5) Bone marrow biopsy needed for definitive diagnosis.

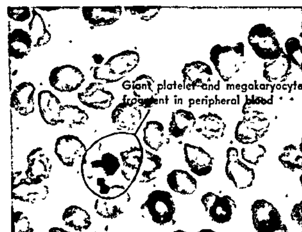
EXTRAMEDULLARY HEMATOPOIESIS



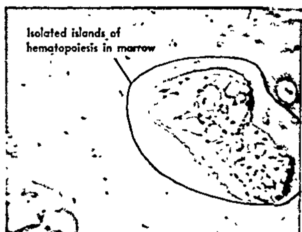
(1)



(2)



(3)



(4)



(5)